~~10/513699~~ 10/518,887 CAPLUS

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13	FEB 26	MEDLINE reloaded with enhancements
NEWS 14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
NEWS 20	MAR 20	MARPAT now updated daily
NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 23	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS 24	APR 02	JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

<12/04/2007> Erich Leese

10/513699

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:52:08 ON 21 APR 2007

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:52:14 ON 21 APR 2007
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STRUCTURE FILE UPDATES: 20 APR 2007 HIGHEST RN 931582-00-2
DICTIONARY FILE UPDATES: 20 APR 2007 HIGHEST RN 931582-00-2

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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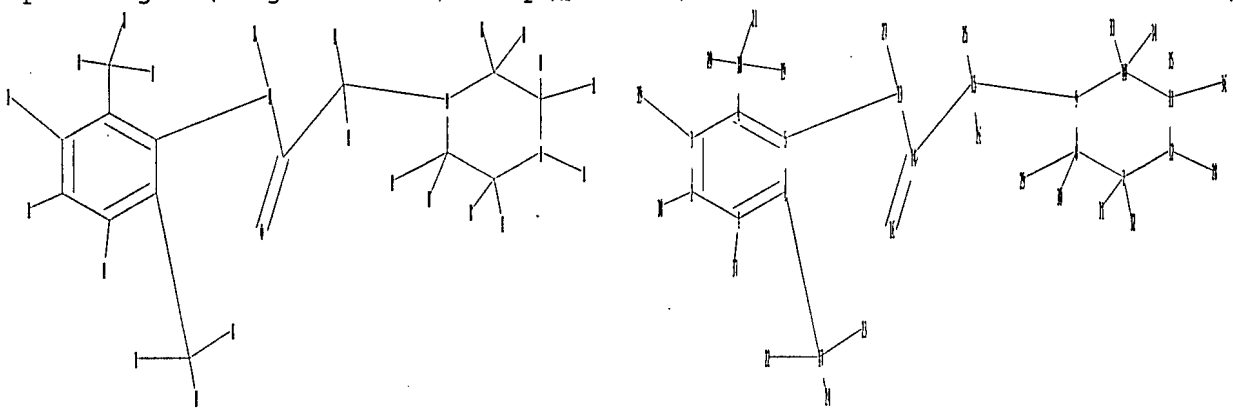
Uploading C:\Program Files\Stnexp\Queries\10518887.str



chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33
34 35 36 37 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-37 2-38 3-39 4-18 5-13 6-17 7-31 7-32 8-29 8-30 9-15 10-33 10-34
11-35 11-36 12-28 13-14 13-27 14-15 14-16 15-25 15-26 17-22 17-23 17-24
18-19 18-20 18-21

<12/04/2007> Erich Leese

ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
5-13 7-8 7-12 8-9 9-10 9-15 10-11 11-12 13-14 14-16
exact bonds :
1-37 2-38 3-39 4-18 6-17 7-31 7-32 8-29 8-30 10-33 10-34 11-35 11-36
12-28 13-27 14-15 15-25 15-26 17-22 17-23 17-24 18-19 18-20 18-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 7 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 13:52:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 162 TO ITERATE

100.0% PROCESSED 162 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2477 TO 4003
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full
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FULL SCREEN SEARCH COMPLETED - 3304 TO ITERATE

100.0% PROCESSED 3304 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L3 2 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'CAPLUS' ENTERED AT 13:52:44 ON 21 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 21 Apr 2007 VOL 146 ISS 18
FILE LAST UPDATED: 20 Apr 2007 (20070420/ED)

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http://www.cas.org/infopolicy.html

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=> s l3 full
L4          34 L3

=> s l3/prep full
            34 L3
       4392036 PREP/RL
L5          17 L3/PREP
                 (L3 (L) PREP/RL)

=> d ibib abs hitstr tot
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L5 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:214799 CAPLUS
DOCUMENT NUMBER: 146:316936
TITLE: Synthesis of ranolazine
INVENTOR(S): Yan, Jie
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1915982	A	20070221	CN 2006-10152726	20060926

PRIORITY APPLN. INFO.: CN 2006-10152726 20060926

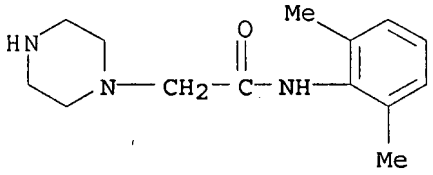
AB The title method comprises the steps of: (1) mixing o-methoxyphenol, dioxane, water and NaOH in a reactor, stirring at room temperature, adding epichlorohydrin, refluxing for 2 h, cooling to room temperature, adding Et acetate, filtering, separating to obtain the organic layer, extracting the water layer with Et acetate twice, mixing the organic layers, drying with anhydrous sodium sulfate, vacuum-distilling, and collecting the fraction at 121-124°C/2 kPa to obtain 3-(2-methoxyphenoxy)-1,2-epoxypropane, (2) mixing 2,6-dimethylaniline, triethylamine and toluene in a reactor, cooling in an ice bath till <0°C, stirring, dripping chloroacetyl chloride, reacting at room temperature for 4 h, washing with 2 N hydrochloric acid twice, separating to obtain the organic layer, drying with anhydrous magnesium sulfate, concentrating, and refining the residue with cyclohexane to obtain 2-chloro-N-(2,6-xylyl)acetamide, (3) mixing 2-chloro-N-(2,6-

xylyl)acetamide, piperazine and anhydrous ethanol in a reactor, heating, refluxing for 4 h, cooling to room temperature, adding aqueous ammonia till pH = 8-9, filtering, extracting the filtrate with methylene dichloride, mixing the extract, washing with water, drying with anhydrous sodium sulfate, concentrating, and refining the residue with ether to obtain N-(2,6-xylyl)-2-(1-piperazine)acetamide, (4) mixing 3-(2-methoxyphenoxy)-1,2-epoxypropane, N-(2,6-xylyl)-2-(1-piperazine)acetamide and methanol in a reactor, refluxing for 3h, and vapor. Ranolazine can be used as antianginal agent.

IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of ranolazine)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1044303 CAPLUS

DOCUMENT NUMBER: 143:416136

TITLE: Synthetic technology of ranolazine

AUTHOR(S): Chen, Xiaolin; Hu, Yongzhou

CORPORATE SOURCE: Zhejiang Medical College, Hangzhou, 310053, Peop. Rep. China

SOURCE: Huaxi Yaoxue Zazhi (2004), 19(3), 191-192
CODEN: HYZAE2; ISSN: 1006-0103

PUBLISHER: Huaxi Yike Daxue Yaoxueyuan

DOCUMENT TYPE: Journal

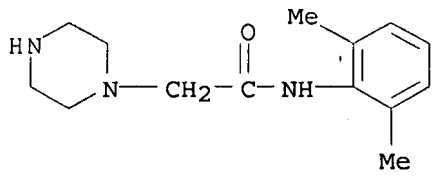
LANGUAGE: Chinese

AB Ranolazine was synthesized and the synthetic process was improved. Ranolazine was synthesized by using 2, 6-dimethylaniline and guaiacol as the starting material followed by 4 step reactions. The overall yields were 36.8%. Chemical structure of the product was confirmed by m.p., IR, 1HNMR and MS. The synthetic route of this method is suitable for industrial production

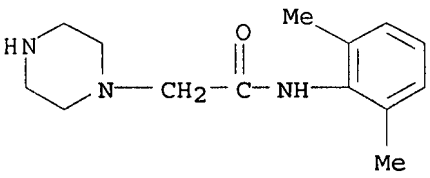
IT 5294-61-1P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic technol. of ranolazine)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:538971 CAPLUS
DOCUMENT NUMBER: 143:369056
TITLE: Synthesis of Ranolazine
AUTHOR(S): Lu, Wenchao; Li, Yingqi; Zhao, Xianglin; Guo, Chun; Zhou, Kai
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, Liaoning Province, 110016, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2004), 35(11), 641-642
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 143:369056
AB Ranolazine was prepared from 2,6-dimethylaniline and 2-chloroacetyl chloride by amidation and subsequent condensation with piperazine to give N-(2,6-dimethylphenyl)-2-(1-piperazinyl)acetamide, which subjected to condensation with 2-(2-methoxyphenoxy)oxirane prepared by condensation of 2-methoxyphenol and epichlorohydrin. The overall yield of ranolazine was 51% (based on 2,6-dimethylaniline).
IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with (methoxyphenoxymethyl)oxirane)
RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)

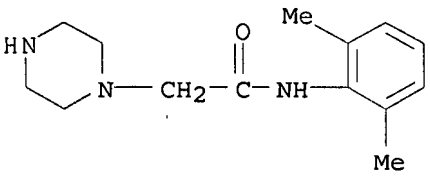


L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:387692 CAPLUS
DOCUMENT NUMBER: 143:151927
TITLE: Chemo-enzymatic synthesis of both enantiomers of the anti-anginal drug ranolazine
AUTHOR(S): Moen, Anders Riise; Karstad, Rasmus; Anthonsen, Thorleif
CORPORATE SOURCE: Department of Chemistry, Norwegian University of Science and Technology, Trondheim, N-7491, Norway
SOURCE: Biocatalysis and Biotransformation (2005), 23(1), 45-51
CODEN: BOBOEQ; ISSN: 1024-2422
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:151927
AB Both enantiomers of the potential anti-anginal drug ranolazine have been synthesized from enantiopure (R)- and (S)-3-chloro-1-(2-methoxyphenoxy)propan-2-ol. These chiral building blocks were produced by kinetic resolution of the corresponding racemic butanoate by hydrolysis

catalyzed by immobilized lipase from Rhizomucor miehei (Lipozyme RM IM) or lipase B from Candida antarctica (Novozym 435). (R)-3-Chloro-1-(2-methoxyphenoxy)propan-2-ol was also made from the racemate in high yield and ee in a stereoinversion reaction.

IT 5294-61-1P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(chemo-enzymic synthesis of both enantiomers of anti-anginal drug ranolazine)

RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



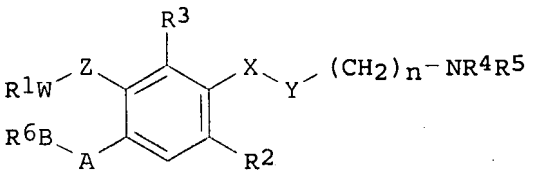
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259820 CAPLUS
DOCUMENT NUMBER: 142:336135
TITLE: Preparation of acetanilides and benzamides for the treatment of asthma and pulmonary inflammation
INVENTOR(S): Baker, William R.; Stasiak, Marcin; Macleod, David
PATENT ASSIGNEE(S): Corus Pharma, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025498	A2	20050324	WO 2004-US28063	20040826

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501137P P 20030908
OTHER SOURCE(S): CASREACT 142:336135; MARPAT 142:336135
GI



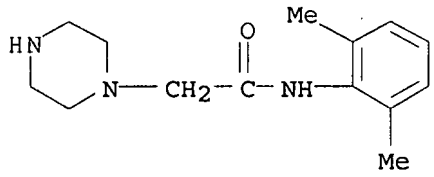
I

AB Title compds. [I; X, Y = NH, O, SO2, CO; n = 1-5; W, Z = H, NH, NR, O, CH2; R = alkyl, (substituted) alkenyl; when Z = H, then R1W is absent and when W is absent, R1 is bonded directly to Z; R6B is absent and when B is absent, R6 is bonded directly to A; R1, R6 = H, alkylheterocyclyl, (substituted) alkylaryl, biaryl, aralkyl, alkoxy, alkoxyalkyl, alkyl, alkenyl, alkoxyaryl, alkylaryl, alkyl; R2, R3 = H, Me; R4, R5 = H, alkyl; R4R5 = atoms to form a (substituted) 2-10 membered ring], were prepared Thus, N-(3-amino-2,6-dimethylphenyl)-2-[1,4']-bipiperidin-1'-ylacetamide (preparation given) was stirred with 6-(4-phenylbutoxy)hexanal and NaBH(OAc)3 in CH2Cl2 at 0-5° to give 2-[1,4']bipiperidin-1'-yl-N-[2,6-dimethyl-3-[6-(4-phenylbutoxy)hexylamino]phenyl]acetamide. The latter inhibited eosinophil survival with IC50 = 5 μM.

IT 5294-61-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acetanilides and benzamides for the treatment of asthma and pulmonary inflammation)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:249685 CAPLUS

DOCUMENT NUMBER: 144:108283

TITLE: Synthesis of a novel antianginal agent Ranolazine

AUTHOR(S): Li, Shu-chun; Huang, He-qing; Li, Zhong-jun

CORPORATE SOURCE: Department of Chemical Biology, School of Pharmaceutical Sciences, Peking University, Beijing, 100083, Peop. Rep. China

SOURCE: Zhongguo Yaowu Huaxue Zazhi (2003), 13(5), 283-285
CODEN: ZYHZEF; ISSN: 1005-0108

PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu

DOCUMENT TYPE: Journal

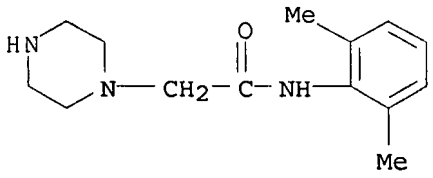
LANGUAGE: Chinese

OTHER SOURCE(S): CASREACT 144:108283

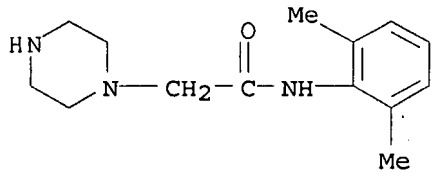
AB Ranolazine, a novel antianginal agent which inhibits partial fatty acid oxidation, reduces myocardial infarct size and cardiac troponin release, was synthesized from o-methoxyphenol, 2,6-dimethylaniline, piperazine and 2,3-epoxypropyl chloride in four steps with good yield. The structure of the product was confirmed by MS, 1H NMR, 13C NMR and element anal.

<12/04/2007> Erich Leese

IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of antianginal agent Ranolazine)
RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:185653 CAPLUS
DOCUMENT NUMBER: 141:225460
TITLE: Synthesis of anti-angina drug ranolazine
AUTHOR(S): Wang, Li-sheng; Feng, Xiao-yu; Zhu, Hong-yuan
CORPORATE SOURCE: Industrial Testing and Experimental Center, Guangxi University, Nanning, 530004, Peop. Rep. China
SOURCE: Guangxi Daxue Xuebao, Ziran Kexueban (2003), 28(4), 301-303
CODEN: GDXZEB; ISSN: 1001-7445
PUBLISHER: Guangxi Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 141:225460
AB Ranolazine as a new anti-angina drug was synthesized from 2,6-dimethylaniline via 3 steps of chloroacetylation, condensation and addition The overall yield is 38.6%.
IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of anti-angina drug ranolazine)
RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:2870 CAPLUS
DOCUMENT NUMBER: 140:59664
TITLE: Condensation process for the production of N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide
INVENTOR(S): Guillaume, Michel Joseph Maurice Andre; Cuypers, Jozef Ludo Jan; Vervest, Ivan Joseph Maria; Leurs, Stefan Marcel Herman; De Smaele, Dirk
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

10/513699

instant case

SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000824	A1	20031231	WO 2003-EP50241	20030619
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2487141	A1	20031231	CA 2003-2487141	20030619
AU 2003255511	A1	20040106	AU 2003-255511	20030619
BR 2003012001	A	20050322	BR 2003-12001	20030619
EP 1517900	A1	20050330	EP 2003-760705	20030619
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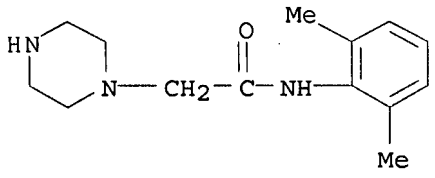
CN 1662517	A	20050831	CN 2003-814667	20030619
JP 2005530837	T	20051013	JP 2004-514875	20030619
US 2005240018	A1	20051027	US 2004-518887	20041221
PRIORITY APPLN. INFO.:			EP 2002-77749 A	20020624
			WO 2003-EP50241 W	20030619

OTHER SOURCE(S): CASREACT 140:59664

AB A process, suitable for industrial exploitation, for the production of N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide (m.p. 118°) is obtained by: (a) reacting piperazine with N-haloacetyl-2,6-xylidine (e.g., N-chloroacetyl-2,6-xylidine) in a molar ratio of 1-6:1, resp., in an aqueous solvent in which has been dissolved an equimolar amount of HCl; (b) separating the solid formed in step (a) from the reaction mixture; (c) neutralizing the filtrate; (d) extracting the filtrate with a solvent which is not or only to a small extent miscible with the aqueous solvent mentioned in step (a); (e) crystallizing the N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide from the solvent mentioned in step (d); and (f) separating the solid obtained in step (e) from the solvent mentioned in step (d).

IT 5294-61-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(condensation process for the production of N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide)

RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)

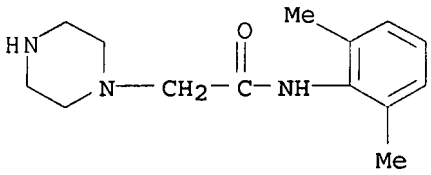


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

<12/04/2007> Erich Leese

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:833036 CAPLUS
DOCUMENT NUMBER: 140:43749
TITLE: Synthesis of T2288: From Bench Synthesis to Pilot Production
AUTHOR(S): Guillaume, Michel; Cuypers, Jef; Vervest, Ivan; De Smaele, Dirk; Leurs, Stef
CORPORATE SOURCE: Chemical Process Research, Johnson & Johnson Pharmaceutical Research and Development, Beerse, 2340, Belg.
SOURCE: Organic Process Research & Development (2003), 7(6), 939-941
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:43749
AB A practical process to make N-(2,6-dimethylphenyl)-2-piperazin-1-yl-acetamide is described, starting from piperazine and N-chloroacetyl-2,6-xylidine. The unwanted N,N'-bis-alkylated product can be removed by simple filtration of the reaction mixture, while the excess of piperazine remains in the aqueous phase after extracting the filtrate with toluene at 70 °C. The product ppts. from the organic phase with 68% active yield.
IT 5294-61-1P
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T2288; production of (dimethylphenyl)piperazinylacetamide from piperazine and chloroacetylxylidine in acidic water)
RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:130020 CAPLUS
DOCUMENT NUMBER: 126:126885
TITLE: Preparation of immunogens and other conjugates of drugs
INVENTOR(S): Lau, Hon-Peng Phillip
PATENT ASSIGNEE(S): Dade Chemistry Systems Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

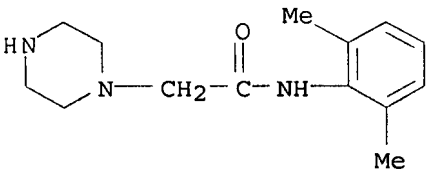
WO 9640664	A2	19961219	WO 1996-US9834	19960607
WO 9640664	A3	19970313		
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9661676	A	19961230	AU 1996-61676	19960607
EP 775128	A1	19970528	EP 1996-919306	19960607
R: DE, ES, FR, IT				
CN 1163612	A	19971029	CN 1996-190885	19960607
JP 10504324	T	19980428	JP 1996-502038	19960607
PRIORITY APPLN. INFO.:			US 1995-473382 A	19950607
			WO 1996-US9834 W	19960607

AB The invention provides a reactive piperazine derivative of dialkyl amino compds., particularly dialkyl amino drugs, for facilitating the conjugation of the drug, directly or through a bifunctional spacer, to a carrier compound, such as proteinaceous materials (e.g. bovine serum albumin, ovalbumin, and keyhole limpet hemocyanin). The drug derivative carrier conjugate can be used as an immunogen for production of antibodies specific to the drug. Addnl., the conjugate can be coupled to a solid support, such as a polymer particle, for use as a particle reagent in immunoassays specific to the drug. N-lidocaine, prepared from piperazine 17.2 g (in EtOAc) and N-chloroacetyl-2,6-xylidine 3.98 g, was conjugated with human serum albumin to obtain a reagent for particle enhanced turbidimetric inhibition immunoassay (PETINIA).

IT 5294-61-1DP, conjugates with proteins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. of dialkyl amino drugs for immunogens and conjugates for immunoassay)

RN 5294-61-1 CAPLUS

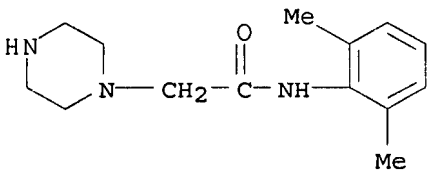
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine derivs. of dialkyl amino drugs for immunogens and conjugates for immunoassay)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



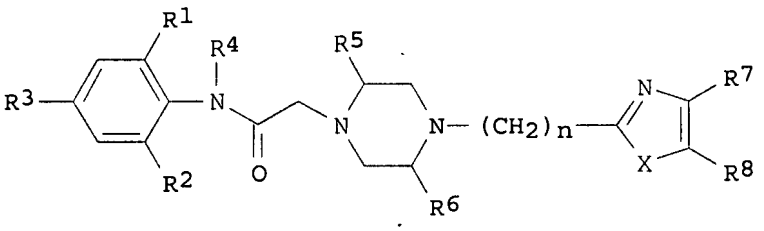
L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

10/513699

ACCESSION NUMBER: 1995:362672 CAPLUS
DOCUMENT NUMBER: 123:169621
TITLE: Adenosine re-uptake inhibiting derivatives of diphenyl oxazoles, thiazoles and imidazoles
INVENTOR(S): Balasubramanian, Neelakantan
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: U.S., 21 pp. Cont.-in-part of U.S. Ser. No. 48, 338, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5382584	A	19950117	US 1994-206572	19940304
ZA 9305153	A	19940201	ZA 1993-5153	19930716
CA 2101311	A1	19940201	CA 1993-2101311	19930726
AT 174913	T	19990115	AT 1993-111910	19930726
ES 2125285	T3	19990301	ES 1993-111910	19930726
NO 9302694	A	19940201	NO 1993-2694	19930727
AU 9344232	A	19940203	AU 1993-44232	19930728
AU 670953	B2	19960808		
HU 67460	A2	19950428	HU 1993-2198	19930728
CN 1085216	A	19940413	CN 1993-109303	19930729
JP 06157472	A	19940603	JP 1993-189947	19930730
JP 3478852	B2	20031215		
HK 1014714	A1	20000721	HK 1998-116045	19981228
PRIORITY APPLN. INFO.:			US 1992-923399 B2	19920731
			US 1993-48338 B2	19930415

OTHER SOURCE(S): CASREACT 123:169621; MARPAT 123:169621
GI



I

AB A series of 1-piperazinyl-N-phenylacetamide derivs. of 4,5-diphenyl-oxazoles, thiazoles, and imidazoles I [wherein R1 and R2 are independently selected from hydrogen, C1-4 alkyl, C1-4 alkoxy, halogen and trifluoromethyl; R3 is hydrogen, halogen, C1-4 alkoxy, nitro or NR9R10 with R9 and R10 being independently selected from hydrogen or C1-4 alkyl, alkanoyl and CO(CH2)nCO2R11; R4 is hydrogen or C1-4 alkyl; R5 and R6 are independently selected from hydrogen, CONR6R10, oxo and CO2R11 with R11 being C1-4 alkyl, or R5 and R6 can be taken together to form a methylene or ethylene bridge; R7 and R8 taken together is a butylene or are both C6H4R12 with R12 being hydrogen, halogen, trifluoromethyl, C1-4 alkyl or C2-4 alkyl-N(R4)2 ; n is zero or an integer from 1 to 4; and X is S, O, or NH] which are novel adenosine transport inhibitors have been found to provide effective antiischemic protection for CNS and cardiac tissue, particularly neurons. A method of treatment to protect against CNS

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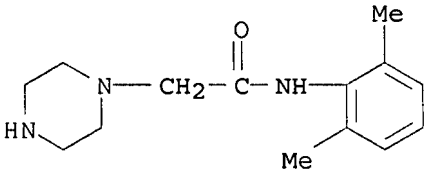
ischemia, such as that resulting from trauma, stroke, or other ischemic conditions, comprises administration of these novel compds. to an individual in need of such treatment. I had IC50 values of less than 10 μM in the adenosine reuptake transport inhibition assay. Pharmaceutical formulations were given.

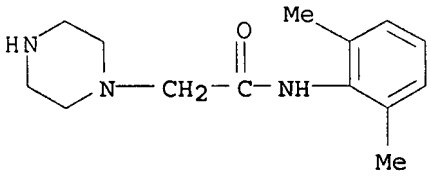
IT 3398-91-2P 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(adenosine re-uptake inhibiting derivs. of diphenyloxazoles, -thiazoles, and -imidazoles)

RN 3398-91-2 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:231018 CAPLUS
DOCUMENT NUMBER: 122:31557
TITLE: Preparation of adenosine re-uptake inhibiting derivatives of diphenyl oxazoles, thiazoles and imidazoles
INVENTOR(S): Neelakantan, Balasubramanian
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

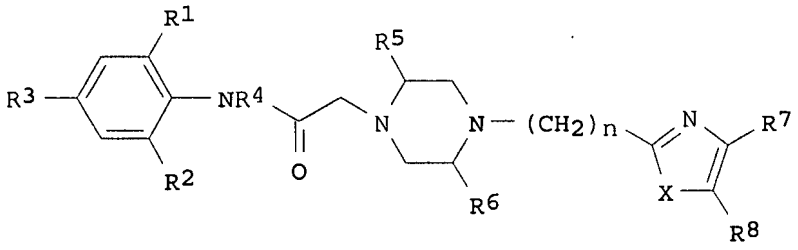
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 582164	A1	19940209	EP 1993-111910	19930726
EP 582164	B1	19981223		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

ZA 9305153	A	19940201	ZA 1993-5153		19930716
CA 2101311	A1	19940201	CA 1993-2101311		19930726
AT 174913	T	19990115	AT 1993-111910		19930726
ES 2125285	T3	19990301	ES 1993-111910		19930726
NO 9302694	A	19940201	NO 1993-2694		19930727
AU 9344232	A	19940203	AU 1993-44232		19930728
AU 670953	B2	19960808			
HU 67460	A2	19950428	HU 1993-2198		19930728
CN 1085216	A	19940413	CN 1993-109303		19930729
JP 06157472	A	19940603	JP 1993-189947		19930730
JP 3478852	B2	20031215			
HK 1014714	A1	20000721	HK 1998-116045		19981228
PRIORITY APPLN. INFO.:			US 1992-923399	A	19920731
			US 1993-48338	A	19930415

OTHER SOURCE(S): CASREACT 122:31557; MARPAT 122:31557

GI



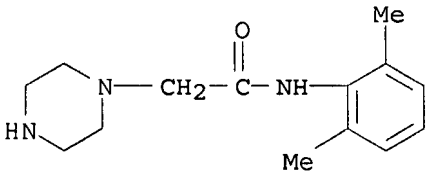
I

AB A series of 1-piperazinyl-N-phenylacetamide derivs. of 4,5-diphenyl-oxazoles, thiazoles, and imidazoles I [R1, R2 = C1-4 alkyl, C1-4 alkoxy, halo, CF3; R3 = H, halo, C1-4 alkoxy, NO2, amino, etc.; R4 = H, C1-4 alkyl; R5, R6 = H, carboxy, etc; R5R6 = CH2, CH2CH2; R7R8 = butylene bridge; R7, R8 = aryl; n = 1-4; X = S, O, NH], which are novel adenosine transport inhibitors (with no data) have been found to provide effective antiischemic protection for CNS tissue, particularly neurons. A method of treatment (with no data) to protect against CNS ischemia, such as that resulting from trauma, stroke, or other ischemic conditions, comprises administration of these novel compds. to an individual in need such treatment. Thus, condensation of 3-aminocarbonyl-N-(2,6-dimethylphenyl)-1-piperazineacetamide (preparation given) with 2-bromomethyl-4,5-diphenyloxazole in the presence of NaI in DMF gave 55% title compound, 3-aminocarbonyl-4-[(4,5-diphenyl-2-oxazolyl)methyl]-N-(2,6-dimethylphenyl)-1-piperazineacetamide.

IT 3398-91-2P 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of diphenyloxazolylalkylpiperazineac
etamide useful for adenosine reuptake inhibitor)

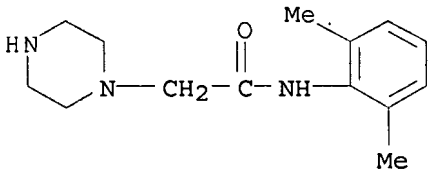
RN 3398-91-2 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

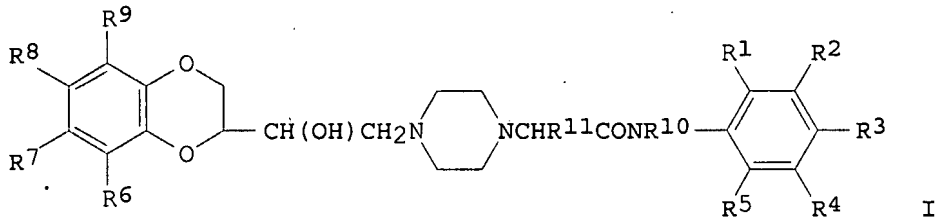
RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:186449 CAPLUS
DOCUMENT NUMBER: 104:186449
TITLE: [(Benzodioxanylhydroxyethyl)piperazinyl]acetanilides which affect calcium entry and β-blockade
INVENTOR(S): Kluge, Arthur F.; Clark, Robin D.; Strosberg, Arthur M.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4558129	A	19851210	US 1983-495870	19830518
PRIORITY APPLN. INFO.:			US 1983-495870	19830518

OTHER SOURCE(S): MARPAT 104:186449
GI



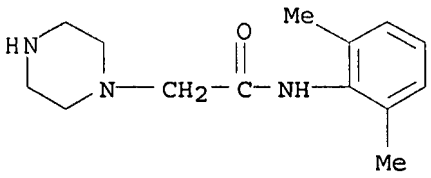
I

AB The title compds. (I; R1-R9 = H, alkyl, CF3, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, halo; R2R3 = OCH2O; R10, R11 = H, alkyl) and their esters and salts, useful as Ca channel blockers and β-adrenergic blockers (no data), were prepared Thus, 2-(bromoacetyl)-1,4-benzodioxan and piperazine were refluxed 6 h in EtOH to give 1-(1,4-benzodioxan-2-yl)-2-(1-piperazinyl)ethanone. This was N-alkylated by ClCH2CONHC6H3Me2-2,6 (prepared by acetylation of the xylidine with ClCH2COCl) and the product reduced with NaBH4 to give (±)-erythro- and (±)-threo-I (R1 = R5 = H, remaining R = H).

IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of, by oxiranylbenzodioxane)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:166777 CAPLUS

DOCUMENT NUMBER: 102:166777

TITLE: Cardioselective aryloxy- and arylthiohydroxypropylpiperazinyl acetanilides which affect calcium entry

INVENTOR(S): Kluge, Arthur Frederick; Clark, Robin Douglas; Strosberg, Arthur Martin; Pascal, Jean Claude; Whiting, Roger Lewis

PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA

SOURCE: Eur. Pat. Appl., 89 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 126449	A1	19841128	EP 1984-105643	19840517
EP 126449	B1	19871223		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4567264	A	19860128	US 1983-495904	19830518
NO 8401968	A	19841119	NO 1984-1968	19840516
NO 163618	B	19900319		
NO 163618	C	19900627		
DK 8402483	A	19841119	DK 1984-2483	19840517
DK 168535	B1	19940418		
FI 8401989	A	19841119	FI 1984-1989	19840517
FI 78479	B	19890428		
FI 78479	C	19890810		
AU 8428346	A	19841122	AU 1984-28346	19840517
AU 566489	B2	19871022		
JP 59219271	A	19841210	JP 1984-97630	19840517

JP 04069151	B	19921105			
HU 34177	A2	19850228	HU 1984-1902		19840517
HU 192404	B	19870629			
ES 532565	A1	19851201	ES 1984-532565		19840517
ZA 8403746	A	19860129	ZA 1984-3746		19840517
CS 246080	B2	19861016	CS 1984-3680		19840517
IL 71863	A	19871030	IL 1984-71863		19840517
PL 142760	B1	19871130	PL 1984-247722		19840517
AT 31533	T	19880115	AT 1984-105643		19840517
PL 143558	B1	19880229	PL 1984-252856		19840517
CA 1256874	A1	19890704	CA 1984-454628		19840517
RU 2071471	C1	19970110	RU 1984-3741049		19840517
CS 246099	B2	19861016	CS 1985-3492		19850515
RU 2083570	C1	19970710	RU 1991-5001933		19911112
PRIORITY APPLN. INFO.:			US 1983-495904	A	19830518
			CS 1984-3680	A3	19840517
			EP 1984-105643	A	19840517

OTHER SOURCE(S): CASREACT 102:166777; MARPAT 102:166777

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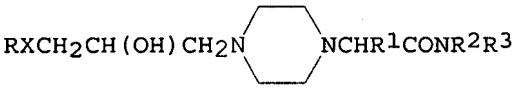
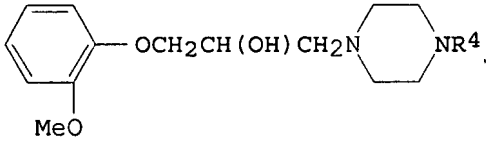


I



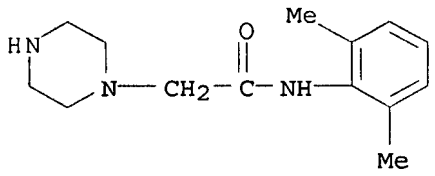
II

AB Hydroxypropylpiperazinylacetanilides I (X = O, S; R = Ph, substituted Ph, benzodioxol-5-yl, 1-naphthyl; R1, R2 = H, alkyl; R3 = Ph, substituted Ph, benzodioxol-5-yl) were prepared Thus, 2-MeOC6H4OH was treated with epichlorohydrin, followed by aminolysis with piperazine to give II (R4 = H). Treatment of 2,6-Me2C6H4NH2 with ClCH2COCl gave 2,6-Me2C6H4NHCOCH2Cl which was treated with II (R4 = H) to give II (R4 = 2,6-Me2C6H4NHCOCH2, III). At 5 μg/kg i.v. III.2HCl gave a significant decrease in S-T segment elevations induced by stress in the electrocardiograms of dogs.

IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with methoxyphenoxyepoxypropane)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



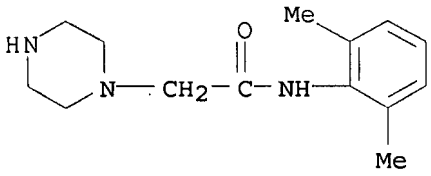
L5 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:171063 CAPLUS

<12/04/2007> Erich Leese

DOCUMENT NUMBER: 82:171063
TITLE: N-Acylpiperazines and piperazine homologs
PATENT ASSIGNEE(S): Ichthyol-Gesellschaft Cordes, Hermanni und Co.
SOURCE: Fr. Demande, 26 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2215236	A1	19740823	FR 1974-2849	19740129
FR 2215236	B1	19771104		
DE 2304155	A1	19740801	DE 1973-2304155	19730129

PRIORITY APPLN. INFO.: DE 1973-2304155 A 19730129
GI For diagram(s), see printed CA Issue.
AB N-acylpiperazines and N-acyldiazepines I (n = 1,2; R = alkylphenyl, alkoxyphenyl, halophenyl, substituted cinnamoyl, phenethyl; R1 = alkyl, allyl, propargyl, substituted anilinoacetyl) and their salts (120 compds) were prepared by acylating the piperazine or diazepine. Thus, 72% I [R = 3,4,5-(MeO)3C6H2, R1 = (CH2)5Me, n = 1] was obtained by treating N-hexylpiperazine with 3,4,5-(MeO)3C6H2COCl. I are coronary vasodilators and effective against coronary insufficiency and cardiac anoxia (no data).
IT 5294-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)
RN 5294-61-1 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:67890 CAPLUS
DOCUMENT NUMBER: 64:67890
ORIGINAL REFERENCE NO.: 64:12704g-h,12705a-h,12706a-h
TITLE: 1,4-Disubstituted piperazines and diazepins
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V.
SOURCE: 26 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6507312		19651210	NL 1965-7312	19650609
BE 664940			BE	
US 3267104			US	

PRIORITY APPLN. INFO.: US 19640609
GI For diagram(s), see printed CA Issue.

AB A series of title compds. of the general formula I was prepared; in formula I, A and A1 are Ph and (or) p-FC6H4 or both are p-MeC6H4 or m-F3CC6H4, A2 represents an arylaminocarbonylalkyl or an arylaminoalkyl group, R = H or Me, and n = 2 or 3. 2,6-Me2C6H3NH2 (121 parts) in 600 parts 40% EtOH treated dropwise with stirring with 55 parts ethylene oxide in 400 parts EtOH, stirred overnight at room temperature, and refluxed 1 hr. yielded 2,6-Me2C6H3NHCH2CH2OH (II), b0.15 100-25°. II (43 parts) and 225 parts 48% HBr stirred 3 hrs. at about 140°, treated with an addnl. 150 parts 48% HBr, and distilled at about 130° to remove during 15 hrs. the H2O, and the residual mixture distilled with 150 parts 48% HBr up to about 160° yielded 2,6-Me2C6H3NHCH2CH2Br.HBr, m. 230-7° (p-MeC6H4)2C:CHCH2CH2Cl (94 parts) in 240 parts iso-PrOH hydrogenated at 35° over 15 parts 10% Pd-C gave (p-MeC6H4)2CH(CH2)3Cl, m.44-6°. 1-[4,4-Bis(p-fluorophenyl)butyl]piperazine (III) (49.5 parts) in 240 parts MeOH treated at about 10° with 20 parts ethylene oxide in 40 parts MeOH, warmed to 40°, and treated 0.5 hr. with gaseous ethylene oxide, and the crude product treated in iso-PrOH-iso-Pr2O with dry HCl yielded 1-[4,4-bis(p-fluorophenyl)butyl]-4-(2-hydroxyethyl)piperazine-2HCl (IV), m. 175-86°. IV (19.5 parts) added in portions to 80 parts SOCl2 and 75 parts CHCl3 and refluxed 3 hrs. gave the 4-ClCH2CH2 analog of IV, m. 210-12° (Me2CO). o-EtCOC6H4NH2 (18 parts) in 105 parts AcOH treated dropwise at 10° with 17 parts ClCH2COCl, stirred 15 min. at 10°, and treated dropwise with 132 parts solution of 51 parts AcONa in 128 parts H2O gave o-EtCOC6H4NHCOCH2Cl (V), m. 76.5-7.5°. Similarly was prepared the m-isomer of V, m. 69.5-70.5°. 2,6-Me2C6H3NHCOCH2Cl 23.8, 1-benzyl-2-methylpiperazine (VI) 19, Na2CO3 32, iso-BuAc 520 parts, and a few crystals iodine refluxed 48 hrs. with stirring gave VII.2HCl (R = PhCH2, R1 = Me, R2 = 2,6-Me2C6H3NHCOCH2, n = 2) (VIII.2HCl), m. 273-4°. Similarly were prepared VII.3HCl (R = PhCH2, R1 = Me, R2 = o-H2NC6H4CH2CH2, n = 2), m. 182-217° (decomposition), and VII.2HCl (R = PhCH2, R1 = H, R2 = 2,6-Me2C6H3NHCOCH2, n = 3) (IX.2HCl), m. 221-30°. VI 19, Na2CO3 32, iso-BuAc 500 parts, and a few crystals iodine refluxed with stirring, treated dropwise with 33.7 parts (p-FC6H4)2CH(CH2)3Cl in 50 parts iso-BuAc, and refluxed 48 hrs. with stirring yielded VII.2HCl [R = PhCH2, R1 = Me, R2 = (p-FC6H4)2CH(CH2)3, n = 2], m. 222-5° (iso-PrOH). Similarly was prepared VII.2HCl [R = PhCH2, R1 = H, R2 = (p-FC6H4)2CH(CH2)3, n = 3], m. 215.4-16.4°. VIII (26 parts) in 2580 parts EtOH hydrogenated at room temperature over 10 parts 5% Pd-C yielded VII (R = H, R1 = Me, R2 = 2,6-Me2C6H3NHCOCH2, n = 2), m. 94-5°. Similarly were prepared VII (R = H, R1 = Me, R2 = PhNHCH2CH2, n = 2), b0.15 119-20°, I (R = R1 = H, R2 = 2,6-Me2C6H3NHCOCH2, n = 3) (X), m. 80-6°, VII [R = H, R1 = Me, R2 = (p-FC6H4)2CH(CH2)3, n = 2], b0.15 170-5°, and VII [R = R1 = H, R2 = (p-FC6H4)2CH(CH2)3, n = 3], b0.05 195-7°. PhNHCH2CH2Br.HBr (202 parts) added in portions during 3 hrs. at room temperature to 494.5 parts piperazine in 2000 parts iso-PrOH and stirred overnight yielded VII (R = R1 = H, R2 = PhNHCH2CH2, n = 2), b0.4-0.5 140-60°; similarly was prepared VII (R = R1 = H, R2 = 2,6-Me2C6H3NHCH2CH2 n = 2), m. 110-14°. Ph2CH(CH2)3Cl 143, piperazine 309, and iso-PrOH 800 parts refluxed 15 hrs. with stirring gave VII [R = R1 = H, R2 = Ph2CH(CH2)3, n = 2], b0.3 177-9°. Similarly were prepared the following VII (R = R1 = H, n = 2) (R2 and b.p./mm. given): Ph(p-FC6H4)CH(CH2)3, 174-80°/0.2; (p-FC6H4)2CH(CH2)3, 192-3°/0.5; (p-MeC6H4)2CH(CH2)3, 180-90°/0.1; (m-CF3C6H4)2CH(CH2)3, 169-71°/0.3. VII.2HCl [R = ClCH2CH2, R1 = H, R2 = (p-FC6H4)2CH(CH2)3, n = 2] 4.6, p-FC6H4NH2 1.3, Et3N 35, and xylene 180 parts refluxed 20 hrs. and diluted with 100 parts H2O yielded VII.3HCl [R = p-FC6H4NHCH2CH2, R1 = H, R2 = (p-FC6H4)2CH(CH2)3, n = 2], m. 221-4° (iso-PrOH). Similarly prepared were VII.3HCl [R = m-MeOC6H4NHCH2CH2, R1 =

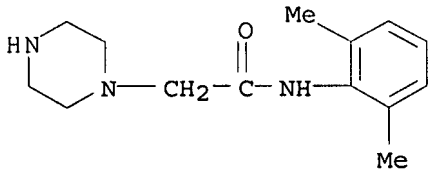
H, R2 = (p-FC6H4)2CH(CH2)3, n = 2], m. 193-4.5°, and VII.·3HCl [R = p-MeOC6H4NHCH2CH2, R1 = H, R2 = (p-FC6H4)2CH(CH2)3, n = 2], m. 219-21°. Ph(p-MeC6H4)CH(CH2)3Cl 2, 1-(2-anilinoethyl)piperazine 1.6, Na2CO3 0.32, iso-BuAc 400 parts, and a few crystals iodine refluxed 90 hrs. with stirring yielded VII.3HCl [R = PhNHCH2CH2, R1 = H, R2 = Ph(p-MeC6H4)CH(CH2)3, n = 2], m. 207-14.5° (decomposition). Similarly were prepared the I listed in the first table. 1-C10H7NHCH2CH2Br.HBr (8.3 parts) in H2O basified with NH4OH and extracted with xylene, and the washed and dried extracted refluxed 24 hrs. with stirring with 16.5 parts III gave after treatment of the product with HCl in Et2O I.2HCl [A = A1 = p-FC6H4, A2 = 2,1-C10H4CH2CH2, R = H, n = 2]. A, A1, A2, R, n, M.p. of salt; p-FC6H4, p-MeC6H4, PhNHCH2CH2, H, 2, 213.5-23° (3HCl); 2-thienyl, p-FC6H4, PhNHCH2CH2, H, 2, 202.5-14.5° (3HCl); p-MeC6H4, p-MeC6H4, PhNHCH2CH2, H, 2, 215-20.5° (3HCl); p-FC6H4, p-MeC6H4, 2,6-Me2C6H3NHCOCH2, H, 2, 250-3° (2HCl); p-FC6H4, p-FC6H4, 2,6-Me2C6H3NHCOCH2, Me, 2, 185-6° (free base); p-FC6H4, p-FC6H4, PhNHCH2CH2, Me, 2, 212-24° (3HCl); p-MeC6H4, p-MeC6H4, 2,6-Me2C6H3NHCOCH2, H, 3, 248.5-51.5° (3HCl); VII [R = R1 = H, R2 = Ph2CH(CH2)3, n = 2] 5.9, PhNHCH2CH2Br.HBr 6.2, Na2CO3 8.5, iso-BuAc 160 parts and a few crystals iodine refluxed 48 hrs., and the product treated in 420 parts iso-Pr2O with dry HCl gave VII 3.HCl [R = PhNHCH2CH2, R1 = H, R2 = Ph2CH-(CH2)3, n = 2] (XI.3HCl), m. 227-9°. Similarly were prepared the following I (A1 = Ph, n = 2) (A, A2, and m.p. of salt or base given): Ph, MePhNCH2CH2, 260-3° (decomposition) (2HCl); Ph, o-MeC6H4NHCOCH2, 223.5-27° (2HCl); Ph, 2,3-Me2C6H3NHCOCH2, 226.5-29° (2HCl); Ph, 2,6-Me2C6H3NHCOCH2, 247-50° (2HCl); Ph, 2,6-Et2C6H3NHCOCH2, 151-5° (2HCl); Ph, 2,5-(MeO)2C6H3NHCOCH2, 100-1° (base); Ph, 1-C10H7NHCOCH2, 160.5-2.5° (base); p-FC6H4, PhNHCH2CH2, 229-30° (3HCl); p-FC6H4, MePhNCH2CH2, 253-6° (2HCl); p-FC6H4, 2,6-Cl2C6H3NHCOCH2, 232-3.5° (2HCl); p-FC6H4, o-MeC6H4NHCOCH2, 218-24° (2HCl); p-FC6H4, 2,3-Me2C6H3NHCOCH2, 239-42° (decomposition) (2HCl); p-FC6H4, 2,5-Me2C6H3NHCOCH2, 246.5-7.5° (2HCl); p-FC6H4, 2,6-Me2C6H3NHCOCH2, 139.5-41° (base); p-FC6H4, 2,6-Et2C6H3NHCOCH2, 235.5-38° (2HCl); p-FC6H4, 2,5-(MeO)2C6H3NHCOCH2, 189.5-92° (2HCl); p-FC6H4, 2,4-(O2N)2C6H3NHCOCH2, 129-31° (base); p-FC6H4, PhNHCOCH2CH2 (XII), 227.5-32.5° (2HCl); p-FC6H4, 1-C10H7NHCOCH2, 217.5-23° (decomposition) (2HCl). Similarly were prepared the following I (A = A1 = p-FC6H4, n = 2) (A2 and m.p. of salt or base given): PhNHCH2CH2 218-22° (3HCl), o-MeC6H4NHCH2CH2 236-8.5° (3HCl.H2O), m-MeC6H4NHCH2CH2 206-10.5° (3HCl), p-MeC6H4NHCH2CH2 223-31° (3HCl), 2,6-Me2C6H3NHCH2CH2 240-1° (3HCl), MePhNCH2CH2 241-3° (decomposition) (2HCl), PhNHCOCH2 240-51° (2HCl), 2,6-Cl2C6H3NHCOCH2 239-43° (2HCl), p-MeC6H4NHCOCH2 234.5-8.5° (2HCl), 2,3-Me2C6H3NHCOCH2 241-2° (decomposition) (2HCl), 2,5-Me2C6H3NHCOCH2 241-4° (2HCl), 2,6-Me2C6H3NHCOCH2 159-61° (base), 2,6-Et2C6H3NHCOCH2 104-5° (base), 2,5-(MeO)2C6H3NHCOCH2 187.5-96° (decomposition) (2HCl), 1-C10H7NHCOCH2 228-37° (decomposition) (2HCl). Similarly were prepared the 3-Me derivs. of the following I (A = A1 = p-FC6H4, n = 2) (same data given): 2,6-Me2C6H3NHCOCH2 239-46° (2HCl), PhNHCH2CH2 234-5° (3HCl), 2,6-ClMeC6H3NHCOCH2 236.5-38° (2HCl), 2,6-Cl2C6H3NHCOCH2 243-5° (decomposition) (2HCl), o-MeC6H4NHCOCH2 218-28.5° (2HCl), 3,4-Me2C6H3NHCOCH2 209-10° (decomposition) (2HCl). Similarly were prepared the following I (A = A1 = p-FC6H4, n = 3) (same data given): 2,6-Me2C6H3NHCOCH2 240-6° (2HCl), 2,6-ClMeC6H3NHCOCH2 145.5-50° (decomposition) (dioxalate), 2,6-Et2C6H3NHCOCH2 186-6.5° (dioxalate), 3,4-Me2C6H3NHCOCH2 182-3.5° (dioxalate), PhNHCH2CH2 173-7° (dioxalate). Similarly prepared were I (n = 2) listed in the 2nd table. XI.HCl 20.8, Ac2O 20, Et3N 56, and

CHCl3 600 parts refluxed 2 hrs. with stirring, and the oily product treated in dry Et2O with dry HCl gave I (A = A1 = Ph, A2 = AcPhNCH2CH2, n = 2), m. 221-3°. A, A1, A2, M.p. of salt or base; p-MeC6H4, p-MeC6H4, 2,6-Me2C6H3NHCOCH2, 143-4° (base); m-CF3C6H4, m-CF3C6H4, 2,6 Me2C6H3NHCOCH2, 224-5.5° (2HCl); p-FC6H4, p-FC6H4, o-AcC6H4NHCOCH2, 192-4° (2HCl); p-FC6H4, p-FC6H4, o-EtCOC6H4NHCOCH2, 162-76° (2HCl); p-FC6H4, p-FC6H4, m-EtCOC6H4, 225.5-27° (2HCl); p-FC6H4, Ph, 3,4-Me2C6H3NHCOCH2, 234.5-36° (2HCl); p-FC6H4, Ph, 2,4-Me2C6H3NHCOCH2, 226-37° (decomposition) (2HCl); p-FC6H4, p-FC6H4, 2,4-Me2C6H3NHCOCH2, 236-9.5° (2HCl); p-FC6H4, Ph, 2,6-Me2C6H3NHCOCH2CH2, 216-17° (2HCl); p-FC6H4, p-FC6H4, 3,4-Me2C6H3NHCOCH2, 234-9° (2HCl); p-FC6H4, p-FC 6H4, 2,6-Br2C6H3NHCOCH2, 252-5° (decomposition) (2HCl); p-FC6H4, Ph, 2,6-Br2C6H3NHCOCH2, 241-4.5° (2HCl); Ph, Ph, 2,6-(MeO)2C6H3NHCOCH2, 115-17° (base); p-FC6H4, p-FC6H4, 2,6-ClMeC6H3NHCOCH2CH2, 220-1° (2HCl); p-FC6H4, Ph, 2,6-(MeO)2C6H3NHCOCH2, 197.5-8.5° (dioxalate); p-FC6H4, p-FC6H4, 2,6-ClMeC6H3NHCOCH2, 229-34° (2HCl); p-FC6H4, Ph, 2,6-ClMeC6H3NHCOCH2, 219-26° (2HCl); Ph, Ph, 2,6-ClMeC6H3NHCOCH2, 223-7.5° (2HCl); p-FC6H4, p-FC6H4, 2,6-(MeO)2C6H3NHCOCH2, 199-9.5° (dioxalate); Similarly were prepared the following I 2.HCl (n = 2) (A, A1, A2, and m.p. given): Ph, Ph, Ph(EtCO)NCH2CH2, 225-6°; p-FC6H4, Ph, AcPhNCH2CH2 198-208°; p-FC6H4, Ph, Ph(EtCO)NCH2CH2 (XIII), 207-10° p-FC6H4, p-FC6H4, AcPhNCH2CH2, 213-15°; p-FC6H4, p-FC6H4, Ph(EtCO)NCH2CH2, 213-28°. XII from 14 parts XII.2HCl in 100 parts tetrahydrofuran refluxed 3 hrs. with stirring with 2.1 parts LiAlH4 in 100 parts tetrahydrofuran, and the crude product treated in 560 parts Et2O with dry HCl yielded I.3HCl [A = Ph, A1 = p-FC6H4, A2 = PhNH(CH2)3, n = 2], m. 247-50.5° (aqueous MeOH). XIII (8 parts) reduced with 1.28 parts LiAlH4 in 90 parts tetrahydrofuran, and the product treated in dry Et2O with dry HCl yielded I.2HCl (A = A1 = Ph, A2 = PhPrNCH2CH2, n = 2), m. 210-13.5° (MeOH). Similarly were prepared the following I.3HCl (A = A1 = p-FC6H4, n = 2) (A2 and m.p. given): EtPhNCH2CH2, 214-16°; PhPrNCH2CH2, 219-26°. The I exhibit antiagiotensine, antihistamine, coronary vasodilator, central nervous system stimulant, anticarragenic, and local anesthetic activity.

IT 5294-61-1P, 1-Piperazineaceto-2',6'-xylidide
RL: PREP (Preparation)
(preparation of)

RN 5294-61-1 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)- (CA INDEX NAME)



L5 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:27552 CAPLUS

DOCUMENT NUMBER: 64:27552

ORIGINAL REFERENCE NO.: 64:5090g-h,5091a-f

TITLE: Neurotropic and psychotropic agents. VIII. 10-(4-Methylpiperazino)-10,11-dihydrodibenzo[b,f]thiepine and analogs. A new group of neuroleptics

<12/04/2007> Erich Leese

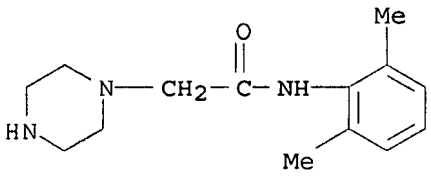
AUTHOR(S): Protiva, M.; Jilek, J. O.; Metysova, J.; Seidlova, V.; Jirkovsky, I.; Metys, J.; Adlerova, E.; Ernest, I.; Pelz, K.; Pomykacek, J.
CORPORATE SOURCE: Pharm. Biochem. Res. Inst., Prague
SOURCE: Farmaco, Edizione Scientifica (1965), 20(10), 721-5
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB cf. CA 63, 8365a. Derivs. of 10-(4-methylpiperazino)-10,11-dihydrodibenzo[b,f]thiepine (perathiepine) (I) were synthesized by modifying I in the piperazine part, in the central 7-membered ring, and in the benzene nuclei. Pharmacol. estimation of I and its derivs. was carried out. I derivs. have the general formula (II). Condensation of 10-chloro-10,11-dihydrodibenzo[b,f]thiepine (III) with 1-(2-hydroxyethyl)piperazine gave 10-[4-(2-hydroxyethyl)-piperazino]-10,11-dihydrodibenzo[b,f]thiepine, m. 108-10° (aqueous EtOH); maleate m. 129-30° (EtOH-ether). III with 1-methylhexahydro-1,4-diazepine gave 10-(4-methylhexahydro-1,4-diazepino)-10,11-dihydrodibenzo[b,f]thiepine, m. 82° (petroleum ether); maleate m. 142° (EtOH). Condensation of the chloro derivs. with 1-(ethoxycarbonyl)piperazine yielded 10-(4-ethoxycarbonylpiperazino)-10,11-dihydrodibenzo[b,f]thiepine (IV), m. 112-14° (EtOH); hydrogen maleate m. 192-3° (aqueous EtOH). Hydrolysis of the amide IV with KOH in ethylene glycol at 180-90° gave 10-piperazino-10,11-dihydrodibenzo[b,f]thiepine (V) m. 104° (acetone); maleate m. 188-90° (aqueous EtOH). Heating V with Et formate in an autoclave at 120-30° gave 10-(4-formylpiperazino)-10,11-dihydrodibenzo[b,f]thiepine (VI) m. 135-6° (EtOH); hydrogen maleate m. 162-4° (EtOH). Reduction of the amide VI with LiAlH4 represents a new synthesis of I, m. 134-5° (MeOH); maleate m. 157-8°. Treatment of the amine V with AcCl in the presence of Na2CO3 yielded the Ac derivative, m. 129-31° (MeOH), reduced similarly to 10-(4-ethylpiperazino)-10,11-dihydrodibenzo[b,f]thiepine m. 85° (petroleum ether); maleate m. 150-1° (EtOH-ether). Chloro derivative of I (II, X = S, R1 or R2 = Cl, R3 = CH3, n = 2), 2,10-dichloro-10,11-dihydrodibenzo[b,f]thiepine, m. 124-4.5°, treated with excess 1-methylpiperazine at 110-20° gave 2-chloro-10-(4-methylpiperazino)-10,11-dihydrobenzo[b,f]thiepine (VII); maleate m. 170.5-71° (EtOH). Similarly 3,10-, 6,10-, 7,10-, and 8,10-dichloro derivs. gave the following isomers of VII (maleates): 3-chloro m. 156-8° (EtOH-ether); 6-chloro m. 163-3.5° (EtOH); 7-chloro m. 183.5-85° (EtOH); 8-chloro (VIII) ("octoclothepine") dihydrochloride, C19H23Cl3N2S, m. 190°. The basic compound of formula II, where X = O, was synthesized from 10,11-dihydrodibenz[b,f]oxepin-10-one. 10-Chloro-10,11-dihydrodibenz[b,f]oxepine, m. 61°, condensed with 1-methylpiperazine at 80° gave 10-(4-methylpiperazino)-10,11-dihydrodibenz[b,f]oxepine; maleate m. 128-30° (EtOH-ether). 10-Chloro-10,11-dihydrodibenzo[a,d]cycloheptene gave by condensation with 1-methylpiperazine 10-(4-methylpiperazino)-10,11-dihydrodibenzo[a,d]cycloheptene; maleate m. 175-6° (EtOH-ether). I dihydrochlorides and I maleates, revealed in mice, rats, and rabbits a strong central depressant action. I reduced also the spontaneous motor activity. The dose, which decreased the animal activity by 50% of the control values, was 156 γ/kg. (base). I was approx. 2-3 times as active as chlorpromazine. I is an effective neuroleptic drug with pronounced antihistamine and antiserotonin actions. VIII dihydrochloride has approx. 3 times higher central depressant activity than I. A high degree of central depressant activity is also shown by

2-chloro-10-(2-dimethylaminoethoxy)-10,11-dihydrobenzo[b,f]thiepine [hydrogen maleate m. 162-5° (acetone-ether)]; 6-chloro analog [hydrogen maleate m. 123.5-25° (EtOH)]; 7-chloro analog [hydrogen maleate m. 114-16° (EtOH)]; 8-chloro analog [hydrogen maleate m. 108-10° (EtOAc)]; 10-(2-dimethylaminoethoxy)-10,11-dihydrodibenz[b,f]oxepine [hydrogen maleate m. 110-13° (EtOH-ether)]; 8-chloro-10-(2-dimethylaminoethoxy)-10,11-dihydrodibenzo[a,d]cycloheptene [hydrogen maleate m. 144-6° (acetone-ether)].

IT 3398-91-2P, 1-Piperazineaceto-2',6'-xylidide, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 3398-91-2 CAPLUS

CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



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L3 2 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:52:44 ON 21 APR 2007
L4 34 S L3 FULL
L5 17 S L3/PREP FULL

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NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13	FEB 26	MEDLINE reloaded with enhancements
NEWS 14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
NEWS 20	MAR 20	MARPAT now updated daily
NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 23	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS 24	APR 02	JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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<12/04/2007> Erich Leese

10/513699

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:08:43 ON 21 APR 2007

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:08:49 ON 21 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 20 APR 2007 HIGHEST RN 931582-00-2
DICTIONARY FILE UPDATES: 20 APR 2007 HIGHEST RN 931582-00-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

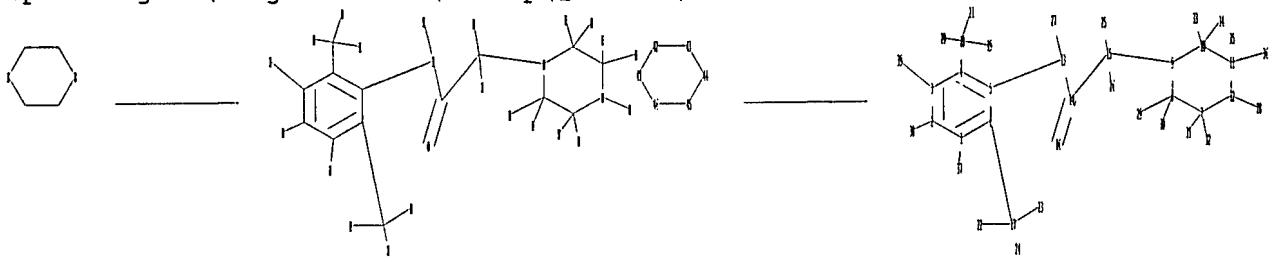
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10518887casreact.str



chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33
34 35 36 37 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 41 42 43 44 45 46
chain bonds :
1-37 2-38 3-39 4-18 5-13 6-17 7-31 7-32 8-29 8-30 9-15 10-33 10-34
11-35 11-36 12-28 13-14 13-27 14-15 14-16 15-25 15-26 17-22 17-23 17-24
18-19 18-20 18-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 41-42 41-46
42-43 43-44 44-45 45-46
exact/norm bonds :
5-13 7-8 7-12 8-9 9-10 9-15 10-11 11-12 13-14 14-16 41-42 41-46 42-43
43-44 44-45 45-46

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exact bonds :
1-37 2-38 3-39 4-18 6-17 7-31 7-32 8-29 8-30 10-33 10-34 11-35 11-36
12-28 13-27 14-15 15-25 15-26 17-22 17-23 17-24 18-19 18-20 18-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 7 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 41:Atom 42:Atom 43:Atom
44:Atom 45:Atom 46:Atom
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 41

L1 STRUCTURE UPLOADED

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.90	1.11

FILE 'CAPLUS' ENTERED AT 14:09:53 ON 21 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 21 Apr 2007 VOL 146 ISS 18
FILE LAST UPDATED: 20 Apr 2007 (20070420/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> file casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.47	1.58

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10/513699

FILE 'CASREACT' ENTERED AT 14:09:59 ON 21 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTENT:1840 - 21 Apr 2007 VOL 146 ISS 18

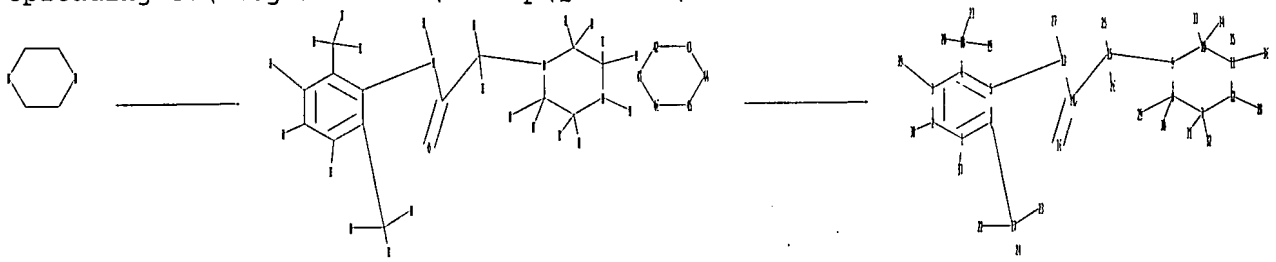
New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
* CASREACT now has more than 12 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
Uploading C:\Program Files\Stnexp\Queries\10518887casreact.str



chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 41 42 43 44 45 46
chain bonds :
1-37 2-38 3-39 4-18 5-13 6-17 7-31 7-32 8-29 8-30 9-15 10-33 10-34 11-35 11-36 12-28 13-14 13-27 14-15 14-16 15-25 15-26 17-22 17-23 17-24 18-19 18-20 18-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 41-42 41-46 42-43 43-44 44-45 45-46
exact/norm bonds :
5-13 7-8 7-12 8-9 9-10 9-15 10-11 11-12 13-14 14-16 41-42 41-46 42-43 43-44 44-45 45-46
exact bonds :
1-37 2-38 3-39 4-18 6-17 7-31 7-32 8-29 8-30 10-33 10-34 11-35 11-36 12-28 13-27 14-15 15-25 15-26 17-22 17-23 17-24 18-19 18-20 18-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 7 :

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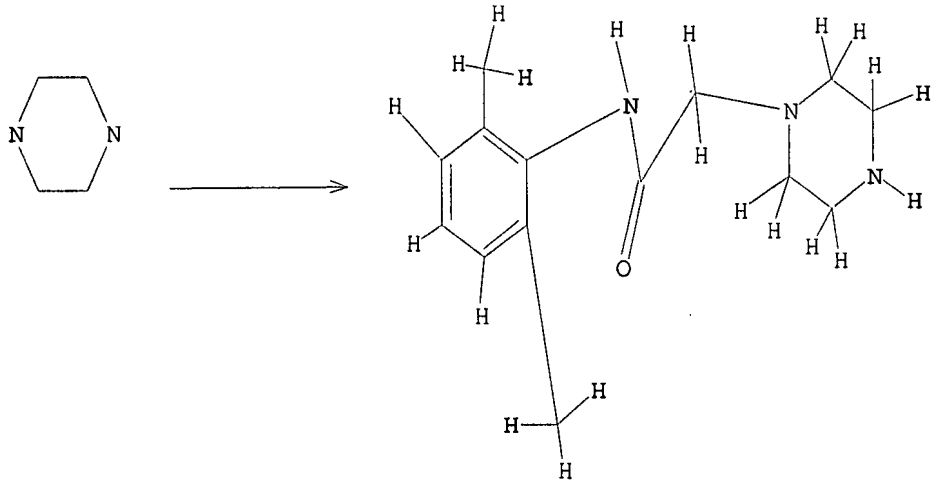
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 41:Atom 42:Atom 43:Atom
44:Atom 45:Atom 46:Atom
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 41

L2 STRUCTURE UPLOADED

=> d l2
L2 HAS NO ANSWERS
L2 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l2
SAMPLE SEARCH INITIATED 14:10:29 FILE 'CASREACT'
SCREENING COMPLETE - 2 REACTIONS TO VERIFY FROM 2 DOCUMENTS

100.0% DONE 2 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L3 0 SEA SSS SAM L2 (0 REACTIONS)

=> s l2 full

```
FULL SEARCH INITIATED 14:10:35 FILE 'CASREACT'
SCREENING COMPLETE -      354 REACTIONS TO VERIFY FROM       36 DOCUMENTS

100.0% DONE     354 VERIFIED      11 HIT RXNS                          7 DOCS
SEARCH TIME: 00.00.01

L4             7 SEA SSS FUL L2 (    11 REACTIONS)

=>  d ibib abs hitstr tot
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number.  SCAN
             must be entered on the same line as DISPLAY, e.g.,
             D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for
             all single-step reactions)
STD -------- BIB, IPC, and NCL

CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first
             hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
             CA reference information (SO, PY).  (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction
             Summary for all hit reactions and fields containing
             hit terms
OCC -------- All hit fields and the number of occurrences of the
             hit terms in each field.  Includes total number of
             HIT, PATH, SPATH reactions. Labels reactions that have
             incomplete verifications.
PATH ------- Reaction Map and Reaction Diagram for the "long
             path".  Displays all hit reactions, except those
```

whose steps are totally included within another hit reaction which is displayed
RX --------- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH, FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):0
'0' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
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SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number. SCAN must be entered on the same line as DISPLAY, e.g., D SCAN.)
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hit terms in each field. Includes total number of
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reaction which is displayed
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RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
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contain a hit substance. Also displays those
multistep reactions that have a hit substance in both
the first and last steps of the reaction, except for
those hit reactions whose steps are totally included
within another hit reaction which is displayed

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ENTER DISPLAY FORMAT (FCRDREF):ibi b
'IBI' IS NOT A VALID FORMAT FOR FILE 'CASREACT'
'B' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
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SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number. SCAN must be entered on the same line as DISPLAY, e.g., D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for all single-step reactions)
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CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with CA reference information (SO, PY). (Default)
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FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction Summary for all hit reactions and fields containing hit terms
OCC -------- All hit fields and the number of occurrences of the hit terms in each field. Includes total number of HIT, PATH, SPATH reactions. Labels reactions that have incomplete verifications.
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ENTER DISPLAY FORMAT (FCRDREF):s l2 full
'S' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB

```
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
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OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number.  SCAN
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```

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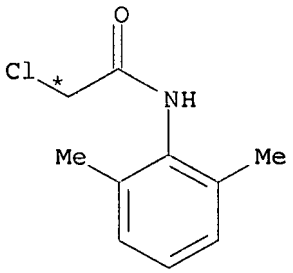
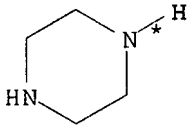
ENTER DISPLAY FORMAT (FCRDREF):hit

L4 ANSWER 1 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

RX(3) OF 17 ...I + L ===> M...

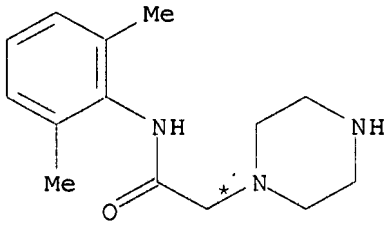


I



L

(3) →



M
YIELD 75%

RX(3) RCT I 1131-01-7, L 110-85-0

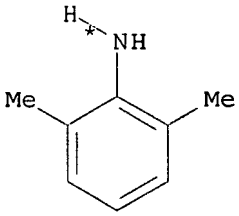
STAGE(1)
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 4 hours, reflux
SUBSTAGE(2) reflux -> room temperature

STAGE(2)
RGT N 7664-41-7 NH3
SOL 7732-18-5 Water
CON pH 8 - 9

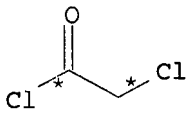
PRO M 5294-61-1

<12/04/2007> Erich Leese

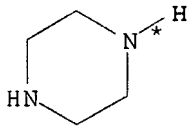
RX(7) OF 17 COMPOSED OF RX(2), RX(3)
RX(7) G + H + L ===> M



G

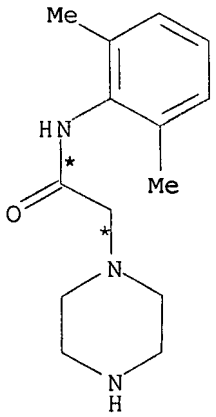


H



L

2
STEPS



M
YIELD 75%

RX(2) RCT G 87-62-7, H 79-04-9
RGT J 121-44-8 Et3N
PRO I 1131-01-7
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 3.5 hours, 0 deg C
SUBSTAGE(3) 0 deg C -> room temperature

RX(3) RCT I 1131-01-7, L 110-85-0

STAGE(1)
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 4 hours, reflux
SUBSTAGE(2) reflux -> room temperature

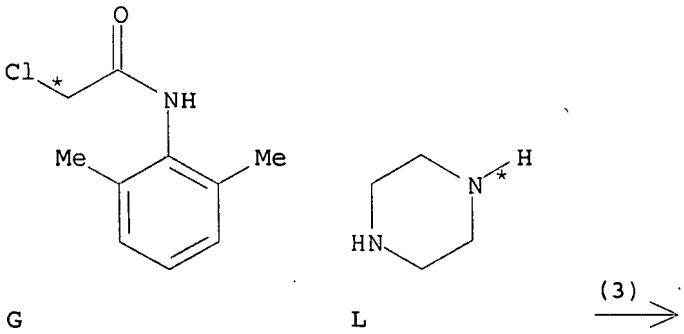
STAGE(2)
RGT N 7664-41-7 NH3
SOL 7732-18-5 Water
CON pH 8 - 9

<12/04/2007> Erich Leese

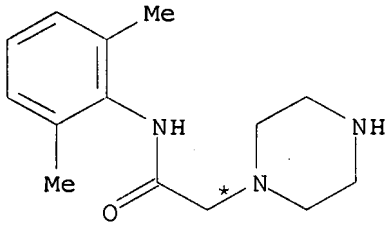
PRO M 5294-61-1

L4 ANSWER 2 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

RX(3) OF 10 ...G + L ===> M...



G L



M
YIELD 61%

RX(3) RCT G 1131-01-7, L 110-85-0

STAGE(1)
SOL 64-17-5 EtOH
CON 3 hours, room temperature -> reflux

STAGE(2)
RGT N 7664-41-7 NH3
SOL 7732-18-5 Water
CON pH 10

PRO M 5294-61-1

RX(6) OF 10 COMPOSED OF RX(2), RX(3)
RX(6) E + F + L ===> M

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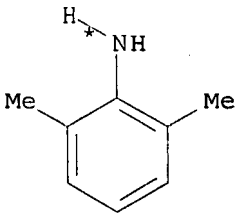
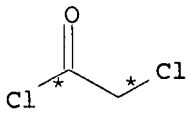
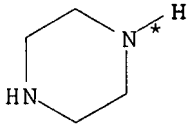


E

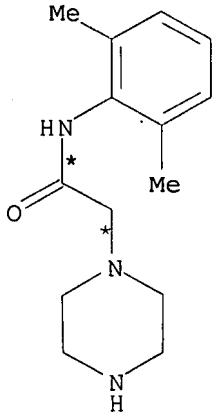


F



L

2 STEPS



M
YIELD 61%

RX(2) RCT E 87-62-7, F 79-04-9

STAGE(1)
RGT H 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 15 minutes, 0 deg C
SUBSTAGE(3) 4 hours, reflux

STAGE(2)
RGT I 7647-01-0 HCl
SOL 7732-18-5 Water
CON pH 3

PRO G 1131-01-7

RX(3) RCT G 1131-01-7, L 110-85-0

STAGE(1)
SOL 64-17-5 EtOH
CON 3 hours, room temperature -> reflux

STAGE(2)
RGT N 7664-41-7 NH3

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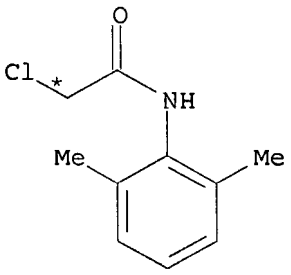
SOL 7732-18-5 Water
CON pH 10

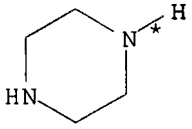
PRO M 5294-61-1

L4 ANSWER 3 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

RX(9) OF 51 ...AH + AJ ===> B...

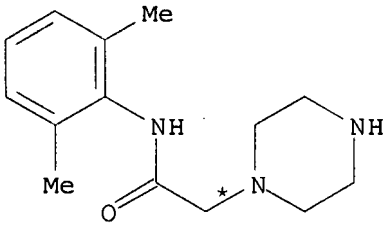


AH



AJ

(9)



B

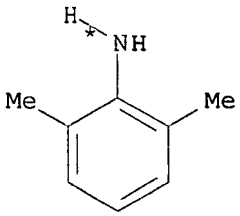
RX(9) RCT AH 1131-01-7, AJ 110-85-0

STAGE(1)
SOL 60-29-7 Et2O
CON 2 hours, reflux

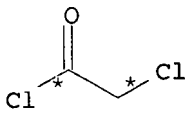
STAGE(2)
RGT AK 7664-41-7 NH3
SOL 7732-18-5 Water

PRO B 5294-61-1

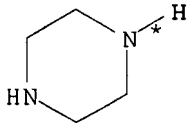
RX(16) OF 51 COMPOSED OF RX(8), RX(9)
RX(16) AF + AG + AJ ===> B



AF

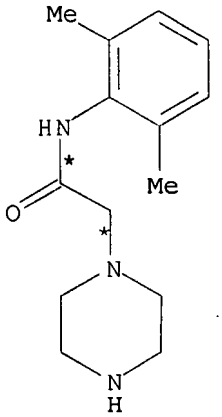


AG



AJ

2 STEPS



B

RX(8) RCT AF 87-62-7, AG 79-04-9
RGT D 497-19-8 Na2CO3
PRO AH 1131-01-7
SOL 108-88-3 PhMe, 7732-18-5 Water
CON SUBSTAGE(1) 2.5 hours, 25 deg C
SUBSTAGE(2) 0 deg C

RX(9) RCT AH 1131-01-7, AJ 110-85-0

STAGE(1)
SOL 60-29-7 Et2O
CON 2 hours, reflux

STAGE(2)
RGT AK 7664-41-7 NH3
SOL 7732-18-5 Water

PRO B 5294-61-1

L4 ANSWER 4 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

RX(57) OF 144 3 A + 2 DY ===> DZ + EA

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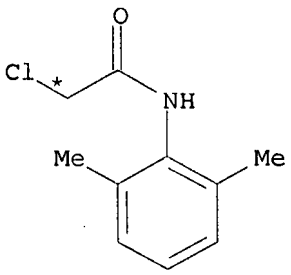
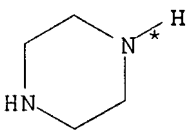
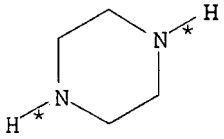


3 A

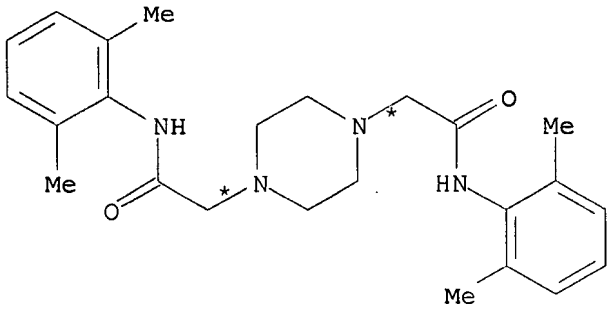


DY

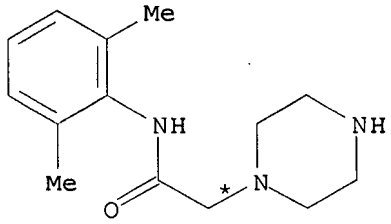


DY

(57)



DZ



EA

RX(57) RCT A 1131-01-7, DY 110-85-0

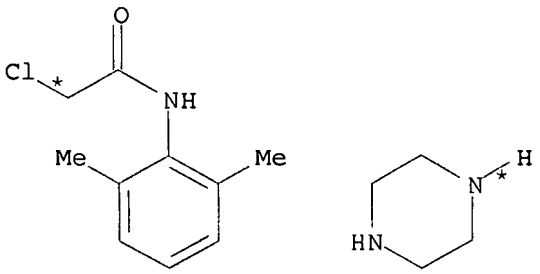
STAGE(1)
RGT EB 497-19-8 Na2CO3
SOL 109-99-9 THF
CON 3 days, room temperature

STAGE(2)
RGT V 1310-58-3 KOH
CON room temperature, basify

PRO DZ 380204-72-8, EA 5294-61-1

L4 ANSWER 5 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

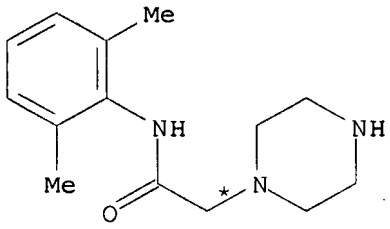
RX(1) OF 10 ...A + B ===> C...



A

B

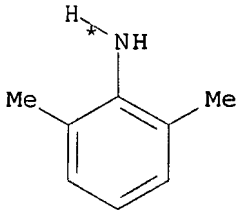
(1)



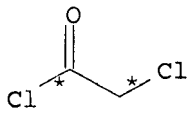
C
YIELD 71%

RX(1) RCT A 1131-01-7, B 110-85-0
PRO C 5294-61-1
SOL 108-88-3 PhMe
CON 3 hours, 80 - 90 deg C

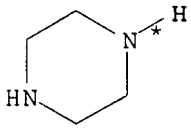
RX(6) OF 10 COMPOSED OF RX(3), RX(1)
RX(6) I + J + B ===> C



I

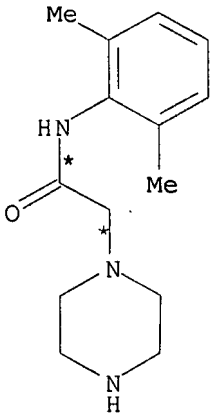


J



B

2
STEPS



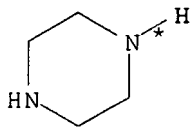
C
YIELD 71%

RX(3) RCT I 87-62-7, J 79-04-9
RGT K 121-44-8 Et3N
PRO A 1131-01-7
SOL 56-23-5 CCl4
CON <30 deg C

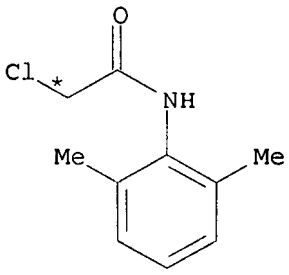
RX(1) RCT A 1131-01-7, B 110-85-0
PRO C 5294-61-1
SOL 108-88-3 PhMe
CON 3 hours, 80 - 90 deg C

L4 ANSWER 6 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

RX(1) OF 1 A + B ===> C

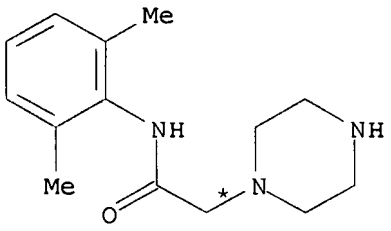


A



B

(1) →



C
YIELD 68%

RX(1) RCT A 110-85-0

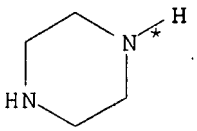
STAGE(1)
RGT D 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature -> 45 deg C
SUBSTAGE(2) 45 deg C -> 25 deg C

STAGE(2)
RCT B 1131-01-7
CON SUBSTAGE(2) 80 deg C
SUBSTAGE(3) 2 hours

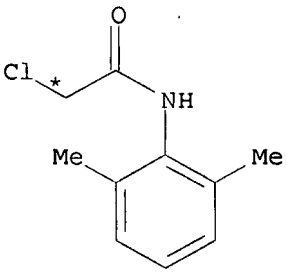
PRO C 5294-61-1
NTE optimization study

L4 ANSWER 7 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

RX(1) OF 1 A + B ===> C

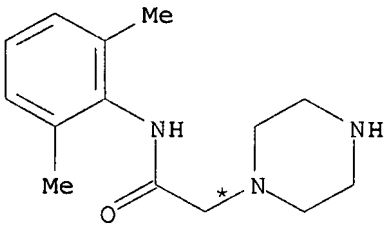


A



B

(1) ⟶



C
YIELD 70%

RX(1) RCT A 110-85-0

STAGE(1)
RGT D 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature -> 45 deg C
SUBSTAGE(2) 45 deg C -> 25 deg C

STAGE(2)
RCT B 1131-01-7
CON SUBSTAGE(1) 25 deg C -> 80 deg C
SUBSTAGE(2) 2 hours, 80 deg C
SUBSTAGE(3) 80 deg C -> 60 deg C

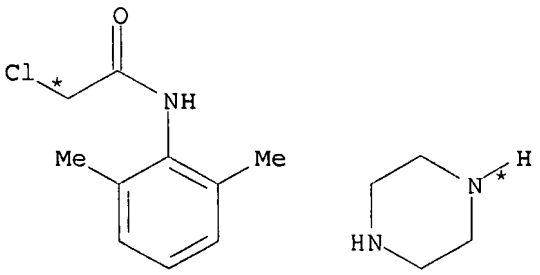
STAGE(3)
RGT E 1310-73-2 NaOH
SOL 7732-18-5 Water
CON 60 deg C, pH >10

PRO C 5294-61-1
NTE safety, optimization study, optimized on solvent,time,stoichiometry,HCl amount, pilot-plant, scalable

=> d ibib abs fhit tot

L4 ANSWER 1 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:108283 CASREACT
TITLE: Synthesis of a novel antianginal agent Ranolazine
AUTHOR(S): Li, Shu-chun; Huang, He-qing; Li, Zhong-jun
CORPORATE SOURCE: Department of Chemical Biology, School of Pharmaceutical Sciences, Peking University, Beijing, 100083, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2003), 13(5), 283-285
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Ranolazine, a novel antianginal agent which inhibits partial fatty acid oxidation, reduces myocardial infarct size and cardiac troponin release, was synthesized from o-methoxyphenol, 2,6-dimethylaniline, piperazine and 2,3-epoxypropyl chloride in four steps with good yield. The structure of the product was confirmed by MS, 1H NMR, 13C NMR and element anal.

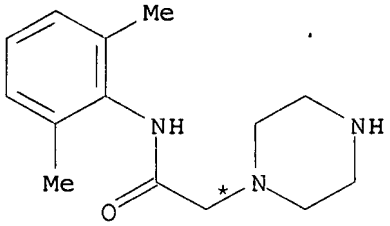
RX(3) OF 17 ...I + L ===> M...



I

L

(3) ⟶



M
YIELD 75%

RX(3) RCT I 1131-01-7, L 110-85-0

STAGE(1)
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 4 hours, reflux
SUBSTAGE(2) reflux -> room temperature

STAGE(2)
RGT N 7664-41-7 NH3
SOL 7732-18-5 Water
CON pH 8 - 9

PRO M 5294-61-1

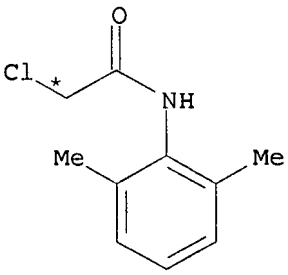
L4 ANSWER 2 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:369056 CASREACT
TITLE: Synthesis of Ranolazine
AUTHOR(S): Lu, Wenchao; Li, Yingqi; Zhao, Xianglin; Guo, Chun; Zhou, Kai
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, Liaoning Province, 110016, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2004), 35(11), 641-642
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu

<12/04/2007> Erich Leese

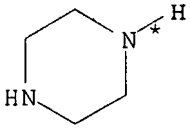
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Ranolazine was prepared from 2,6-dimethylaniline and 2-chloroacetyl chloride by amidation and subsequent condensation with piperazine to give N-(2,6-dimethylphenyl)-2-(1-piperazinyl)acetamide, which subjected to condensation with 2-(2-methoxyphenoxy)oxirane prepared by condensation of 2-methoxyphenol and epichlorohydrin. The overall yield of ranolazine was 51% (based on 2,6-dimethylaniline).

RX(3) OF 10 ...G + L ===> M...

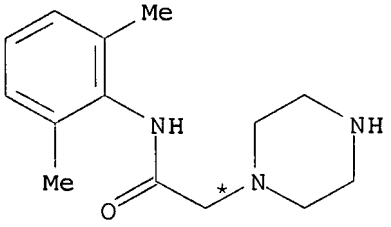


G



L

(3) →



M
YIELD 61%

RX(3) RCT G 1131-01-7, L 110-85-0

STAGE(1)
SOL 64-17-5 EtOH
CON 3 hours, room temperature -> reflux

STAGE(2)
RGT N 7664-41-7 NH3
SOL 7732-18-5 Water
CON pH 10

PRO M 5294-61-1

L4 ANSWER 3 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:151927 CASREACT
TITLE: Chemo-enzymatic synthesis of both enantiomers of the

anti-anginal drug ranolazine

AUTHOR(S): Moen, Anders Riise; Karstad, Rasmus; Anthonsen, Thorleif

CORPORATE SOURCE: Department of Chemistry, Norwegian University of Science and Technology, Trondheim, N-7491, Norway

SOURCE: Biocatalysis and Biotransformation (2005), 23(1), 45-51
CODEN: BOBOEQ; ISSN: 1024-2422

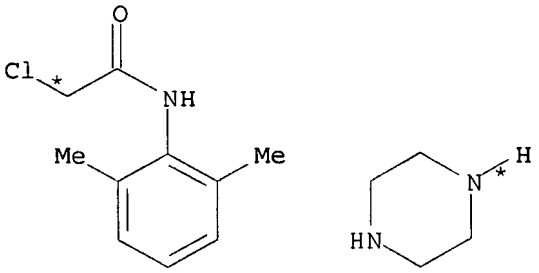
PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal

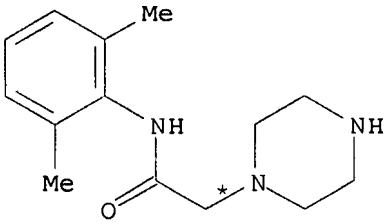
LANGUAGE: English

AB Both enantiomers of the potential anti-anginal drug ranolazine have been synthesized from enantiopure (R)- and (S)-3-chloro-1-(2-methoxyphenoxy)propan-2-ol. These chiral building blocks were produced by kinetic resolution of the corresponding racemic butanoate by hydrolysis catalyzed by immobilized lipase from Rhizomucor miehei (Lipozyme RM IM) or lipase B from Candida antarctica (Novozym 435). (R)-3-Chloro-1-(2-methoxyphenoxy)propan-2-ol was also made from the racemate in high yield and ee in a stereoinversion reaction.

RX(9) OF 51 ...AH + AJ ===> B...



AH AJ



B

RX(9) RCT AH 1131-01-7, AJ 110-85-0

STAGE(1)
SOL 60-29-7 Et2O
CON 2 hours, reflux

STAGE(2)

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RGT AK 7664-41-7 NH3
SOL 7732-18-5 Water

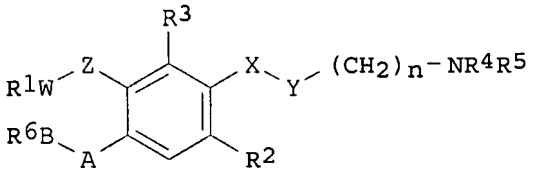
PRO B 5294-61-1
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:336135 CASREACT
TITLE: Preparation of acetanilides and benzamides for the treatment of asthma and pulmonary inflammation
INVENTOR(S): Baker, William R.; Stasiak, Marcin; Macleod, David
PATENT ASSIGNEE(S): Corus Pharma, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025498	A2	20050324	WO 2004-US28063	20040826

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501137P 20030908
OTHER SOURCE(S): MARPAT 142:336135
GI



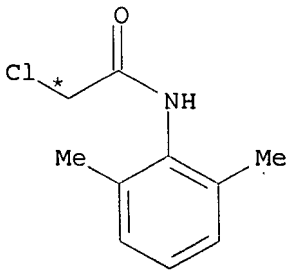
I

AB Title compds. [I; X, Y = NH, O, SO2, CO; n = 1-5; W, Z = H, NH, NR, O, CH2; R = alkyl, (substituted) alkenyl; when Z = H, then R1W is absent and when W is absent, R1 is bonded directly to Z; R6B is absent and when B is absent, R6 is bonded directly to A; R1, R6 = H, alkylheterocyclyl, (substituted) alkylaryl, biaryl, aralkyl, alkoxy, alkoxyalkyl, alkyl, alkenyl, alkoxyaryl, alkylaryl, alkyl; R2, R3 = H, Me; R4, R5 = H, alkyl; R4R5 = atoms to form a (substituted) 2-10 membered ring], were prepared Thus, N-(3-amino-2,6-dimethylphenyl)-2-[1,4']-bipiperidin-1'-ylacetamide (preparation given) was stirred with 6-(4-phenylbutoxy)hexanal and NaBH(OAc)3

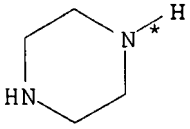
<12/04/2007> Erich Leese

in CH2Cl2 at 0-5° to give 2-[1,4']bipiperidin-1'-yl-N-[2,6-dimethyl-3-[6-(4-phenylbutoxy)hexylamino]phenyl]acetamide. The latter inhibited eosinophil survival with IC50 = 5 μM.

RX(57) OF 144 3 A + 2 DY ===> DZ + EA



3 A



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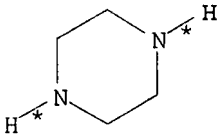
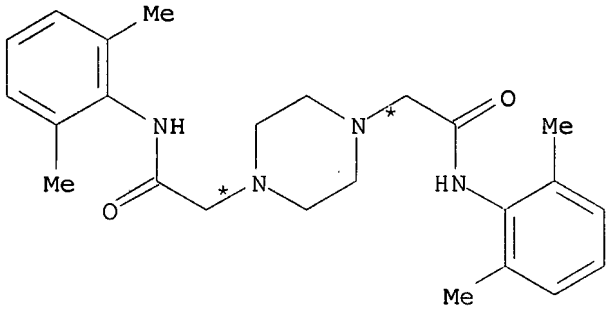
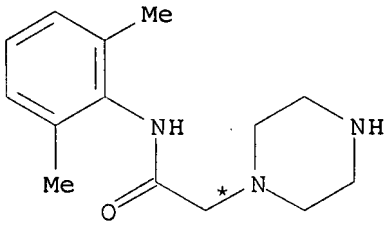


DY

(57)



DZ



EA

RX(57) RCT A 1131-01-7, DY 110-85-0

STAGE(1)
RGT EB 497-19-8 Na2CO3
SOL 109-99-9 THF
CON 3 days, room temperature

STAGE(2)
RGT V 1310-58-3 KOH
CON room temperature, basify

PRO DZ 380204-72-8, EA 5294-61-1

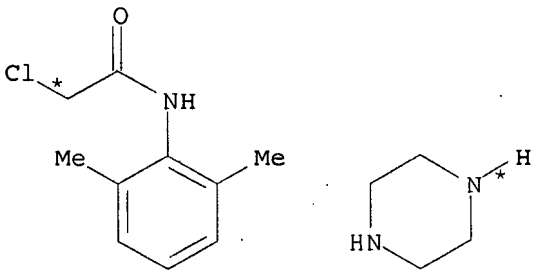
L4 ANSWER 5 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:225460 CASREACT
TITLE: Synthesis of anti-angina drug ranolazine
AUTHOR(S): Wang, Li-sheng; Feng, Xiao-yu; Zhu, Hong-yuan
CORPORATE SOURCE: Industrial Testing and Experimental Center, Guangxi University, Nanning, 530004, Peop. Rep. China

<12/04/2007> Erich Leese

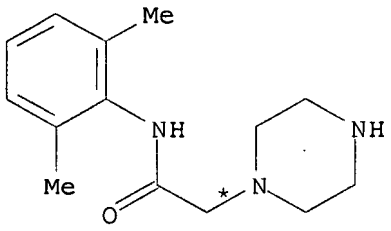
SOURCE: Guangxi Daxue Xuebao, Ziran Kexueban (2003), 28(4), 301-303
CODEN: GDXZEB; ISSN: 1001-7445
PUBLISHER: Guangxi Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Ranolazine as a new anti-angina drug was synthesized from 2,6-dimethylaniline via 3 steps of chloroacetylation, condensation and addition The overall yield is 38.6%.

RX(1) OF 10 ...A + B ===>. C...



A B



C
YIELD 71%

RX(1) RCT A 1131-01-7, B 110-85-0
PRO C 5294-61-1
SOL 108-88-3 PhMe
CON 3 hours, 80 - 90 deg C

L4 ANSWER 6 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:59664 CASREACT
TITLE: Condensation process for the production of N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide
INVENTOR(S): Guillaume, Michel Joseph Maurice Andre; Cuypers, Jozef Ludo Jan; Vervest, Ivan Joseph Maria; Leurs, Stefan Marcel Herman; De Smaele, Dirk
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2

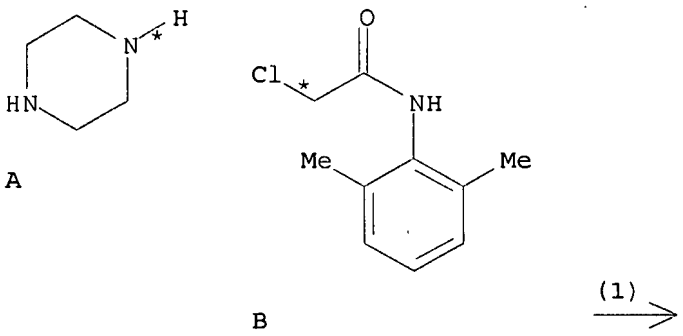
<12/04/2007> Erich Leese

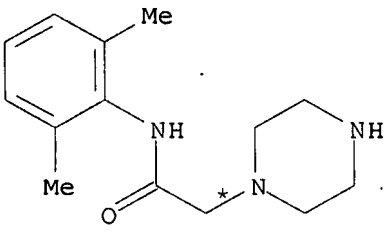
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000824	A1	20031231	WO 2003-EP50241	20030619
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2487141	A1	20031231	CA 2003-2487141	20030619
AU 2003255511	A1	20040106	AU 2003-255511	20030619
BR 2003012001	A	20050322	BR 2003-12001	20030619
EP 1517900	A1	20050330	EP 2003-760705	20030619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1662517	A	20050831	CN 2003-814667	20030619
JP 2005530837	T	20051013	JP 2004-514875	20030619
US 2005240018	A1	20051027	US 2004-518887	20041221
PRIORITY APPLN. INFO.:			EP 2002-77749	20020624
			WO 2003-EP50241	20030619

AB A process, suitable for industrial exploitation, for the production of N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide (m.p. 118°) is obtained by: (a) reacting piperazine with N-haloacetyl-2,6-xylidine (e.g., N-chloroacetyl-2,6-xylidine) in a molar ratio of 1-6:1, resp., in an aqueous solvent in which has been dissolved an equimolar amount of HCl; (b) separating the solid formed in step (a) from the reaction mixture; (c) neutralizing the filtrate; (d) extracting the filtrate with a solvent which is not or only to a small extent miscible with the aqueous solvent mentioned in step (a); (e) crystallizing the N-[(2,6-dimethylphenyl)-2-piperazin-1-yl]acetamide from the solvent mentioned in step (d); and (f) separating the solid obtained in step (e) from the solvent mentioned in step (d).

RX(1) OF 1 A + B ===> C





C
YIELD 68%

RX(1) RCT A 110-85-0

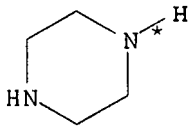
STAGE(1)
RGT D 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature -> 45 deg C
SUBSTAGE(2) 45 deg C -> 25 deg C

STAGE(2)
RCT B 1131-01-7
CON SUBSTAGE(2) 80 deg C
SUBSTAGE(3) 2 hours

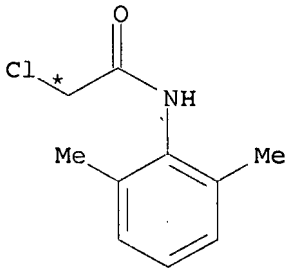
PRO C 5294-61-1
NTE optimization study
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:43749 CASREACT
TITLE: Synthesis of T2288: From Bench Synthesis to Pilot Production
AUTHOR(S): Guillaume, Michel; Cuypers, Jef; Vervest, Ivan; De Smaele, Dirk; Leurs, Stef
CORPORATE SOURCE: Chemical Process Research, Johnson & Johnson Pharmaceutical Research and Development, Beerse, 2340, Belg.
SOURCE: Organic Process Research & Development (2003), 7(6), 939-941
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A practical process to make N-(2,6-dimethylphenyl)-2-piperazin-1-yl-acetamide is described, starting from piperazine and N-chloroacetyl-2,6-xylidine. The unwanted N,N'-bis-alkylated product can be removed by simple filtration of the reaction mixture, while the excess of piperazine remains in the aqueous phase after extracting the filtrate with toluene at 70 °C. The product ppts. from the organic phase with 68% active yield.

RX(1) OF 1 A + B ===> C

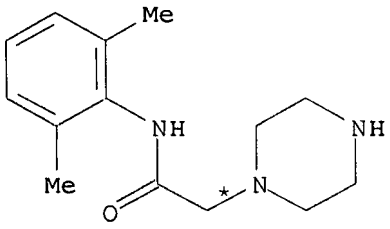


A



B

(1) →



C
YIELD 70%

RX(1) RCT A 110-85-0

STAGE(1)
RGT D 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature -> 45 deg C
SUBSTAGE(2) 45 deg C -> 25 deg C

STAGE(2)
RCT B 1131-01-7
CON SUBSTAGE(1) 25 deg C -> 80 deg C
SUBSTAGE(2) 2 hours, 80 deg C
SUBSTAGE(3) 80 deg C -> 60 deg C

STAGE(3)
RGT E 1310-73-2 NaOH
SOL 7732-18-5 Water
CON 60 deg C, pH >10

PRO C 5294-61-1
NTE safety, optimization study, optimized on solvent,time,stoichiometry,HCl amount, pilot-plant, scalable

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

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L1              STRUCTURE UPLOADED

     FILE 'CAPLUS' ENTERED AT 14:09:53 ON 21 APR 2007

     FILE 'CASREACT' ENTERED AT 14:09:59 ON 21 APR 2007
L2              STRUCTURE UPLOADED
L3            0 S L2
L4            7 S L2 FULL

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   178.14     179.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -5.11      -5.11

STN INTERNATIONAL LOGOFF AT 14:13:05 ON 21 APR 2007
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